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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,948	01/26/2006	Fumihiko Watanabe	20050.1USWO	8441

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EXAMINER	
GALLIS, DAVID E	
ART UNIT	PAPER NUMBER
1625	
MAIL DATE	DELIVERY MODE
08/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,948	WATANABE ET AL.	
	Examiner	Art Unit	
	DAVID E. GALLIS	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2006 and 06 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/26/06 and 4/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

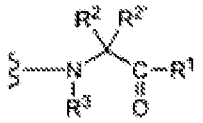
DETAILED ACTION

1. Claims 1 through 17 are pending. Claims 3, 4, 5, 7, 8, 9 and 12 through 16 have been amended Claim 17 has been newly added. Applicants' claim to foreign priority by application JAPAN 2003-282354 filed July 30, 2003 is acknowledged.

Election/Restrictions

2. Applicants' election of Group III, claims 1 through 9, 12 through 14 and 7 is acknowledged. Applicant states that election was made without traverse, therefore the election is hereby MADE FINAL. The examiner, however, has rejoined Groups I, II and IV through X comprising all pending claims and predicated on the elected Group III subject matter. The examined subject matter is as follows:

> Claims 1 through 17 drawn to compounds of formulas (I), (II-A) and (II-B), their pharmaceutical compositions, use in a method of treating metalloproteinase related disease, wherein W represents the group below and R^1 through R^{21} carry the limitations recited in claim 1, classified in various classes and various subclasses.



Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 through 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R^6 moieties comprising phenyl, naphthyl, furanyl, thiophenyl, and cyclohexyl, and phenylene R^4 linkages, does not reasonably provide enablement for R^6 moieties comprising pyridinyl, quinolinyl or all heterocyclic moieties in general, and heteroarylene R^4 linkages. Furthermore, the specification is not enabling for the treatment of all disease "caused by or related to metalloproteinase" as claimed in claim 16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

5. Claims 1 through 17, drawn to compounds of formulas (I), (II-A) and (II-B) comprising R^6 moieties comprising pyridinyl, quinolinyl or all heterocyclic moieties in general, and heteroarylene R^4 linkages are only addressed synthetically by general equation. These groups are significantly different from the phenyl, naphthyl, furanyl, thiophenyl, and cyclohexyl terminal moieties and phenylene linkage that are likewise described and clearly exemplified. It is not obvious by way of the disclosure how a heteroarylene linkage would behave toward the formation of, or reaction with, an aldoxime (see ¶0028, step 2; ¶0032, step 3). Claim 16, drawn to a method of treating "disease caused by or related to metalloproteinase", is not enabling for the treatment such diverse disease. Page 1 of the specification indicates those diseases include to such diverse diseases as arthritis, corneal ulcers, periodontal disease, tumor metastatis, and viral infection including HIV infection. However, the specification provides no

guidance as to how such different diseases might be treated by a formula (I) compound; all that is provided is *in vitro* evidence of metalloproteinase inhibition. Experiments to test the possible usefulness of these compounds in animal models are described on pages 22 through 29, but are not actually performed. The prior art fails to provide compensatory guidance; Tamura et al. (cited by applicants) indicates only an association of some metalloproteinases with cancer. Thus without further direction it would require undue experimentation to practice the invention of claim 16 as broadly claimed

"The factors to be considered in making an enablement rejection have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Determination of the effects of these linkage groups and terminal groups on the synthesis of the claimed compounds, as well as a method of treating disease caused by or related to metalloproteinase, would require extensive experimentation. b) The direction concerning the inclusion of these linkage groups and terminal groups is found in the disclosure on page 18 through 20, wherein there is no specific reference to pyridinyl, quinolinyl or all heterocyclic terminal moieties in general, and heteroarylene R^4 linkages. Information related to treatment of all disease caused by or related to metalloproteinase is found on pages 22 through 29. c) There is no disclosed working

example of the incorporation of pyridinyl, quinolinyl or all heterocyclic moieties in general, nor is there an actual animal based experiment performed enabling treatment for disease caused by or related to metalloproteinase. d) The nature of the invention is organic and medicinal chemistries. e) The state of the art currently lacks any single method that extrapolates the effects of a phenylene or phenyl group across all heterocyclic groups and linkages in a reaction mechanism, nor does the state of the art demonstrate the claimed compound as a class effective toward the treatment of all disclosed diseases. f) Artisans making Applicants' invention would require a Ph.D. in synthetic organic chemistry and many years of experience hetercyclic and clinical chemistry. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and the effects of varied hetero elements on the reactivity of functional group is considered to be an unpredictable factor. h) The breadth of the R^6 terminal groups and R^4 linkages are of a speculative nature, and as evidenced by their absence as any working example, are molecular attributes that Applicants intend to use, but have not been attempted. Neither the instant disclosure nor referenced literature support the inclusion of these terminal groups or linkages in compounds of formulas (I), (II-A) and (II-B). Furthermore, the breath of the claimed treatment of disease caused by or related to metalloproteinase is speculative, and as yet, unattempted.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 15 provides for the use of compound of formula (I), but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 15 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David E. Gallis whose telephone number is 571-272-9068. The examiner can normally be reached on Mon-Thur 8:30-7:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Andres/
Supervisory Patent Examiner, Art Unit 1625

David E. Gallis
Patent Examiner